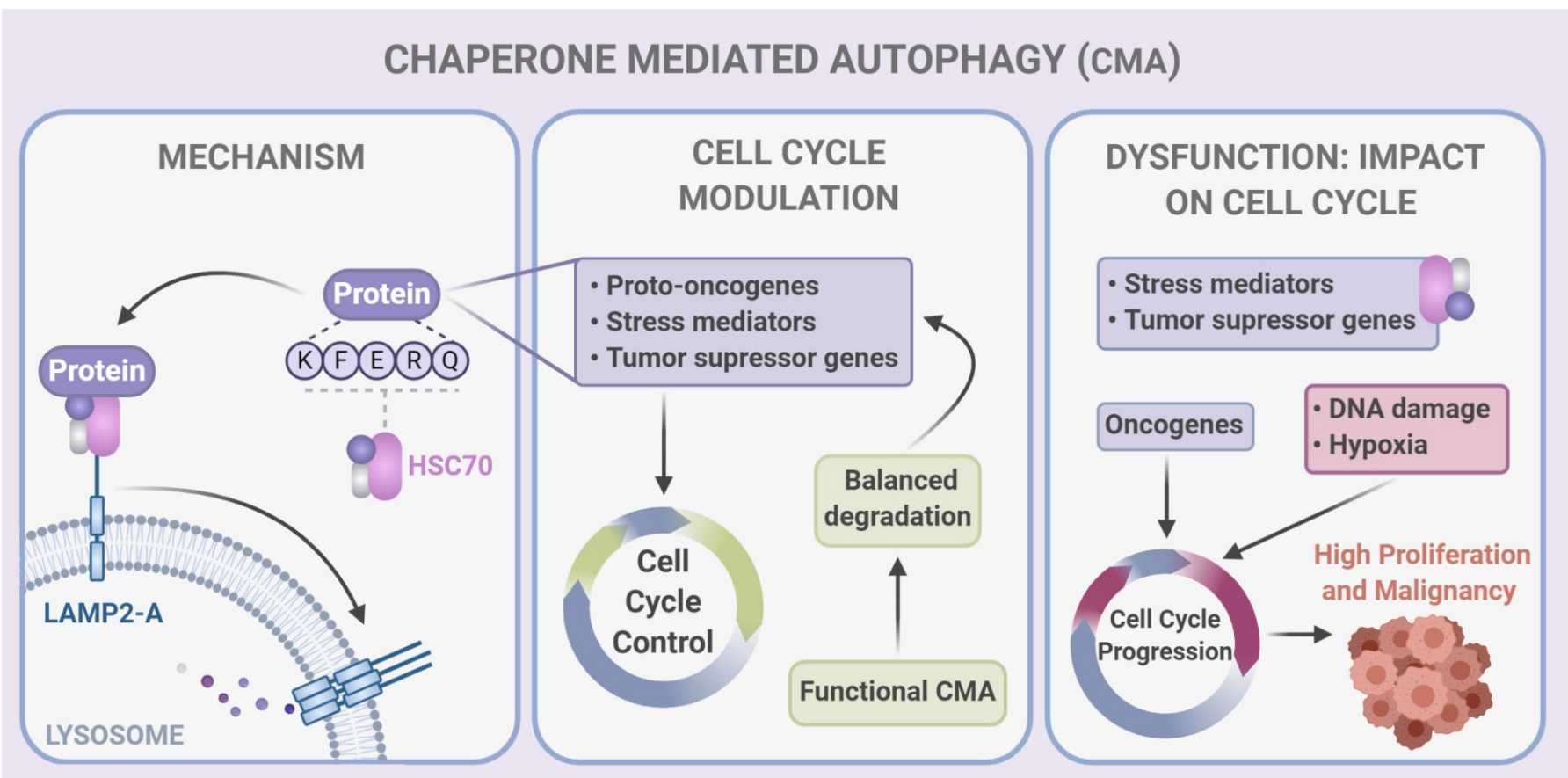


## Background & Objective

### Background

Temozolomide (TMZ) is the first option of chemotherapy for glioblastoma (GBM), while its efficacy is limited due to unsatisfying treatment response and tumor relapse. The interplay between TMZ and autophagy was suggested to play a role in the process of treatment [1]. As a selective form of autophagy, Chaperon-mediated autophagy (CMA) maintains cellular homeostasis through degradation of substrate proteins [2] and remains poorly understood in GBM. Evaluating the autophagic response of GBM cells to TMZ treatment may provide more insights for drug-autophagy interaction.



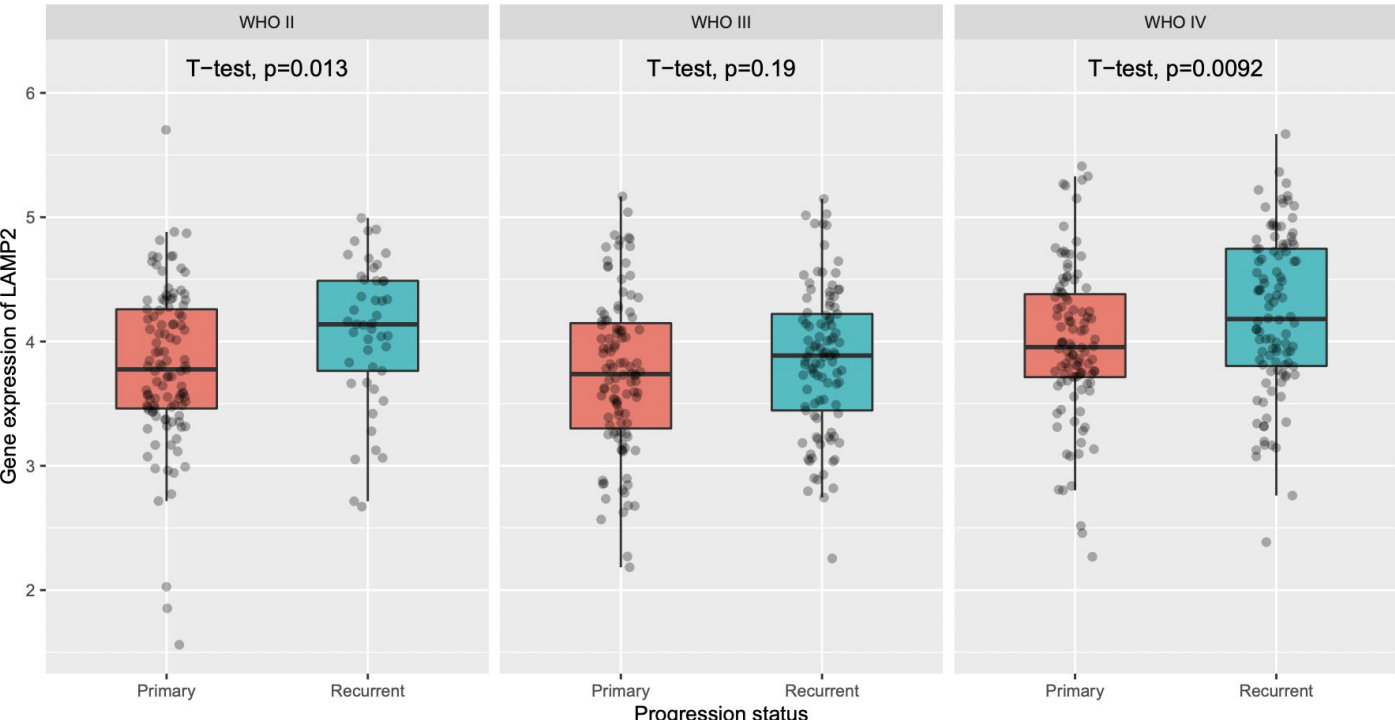
**Objective:** To investigate the effect of TMZ on CMA in GBM

## Methods

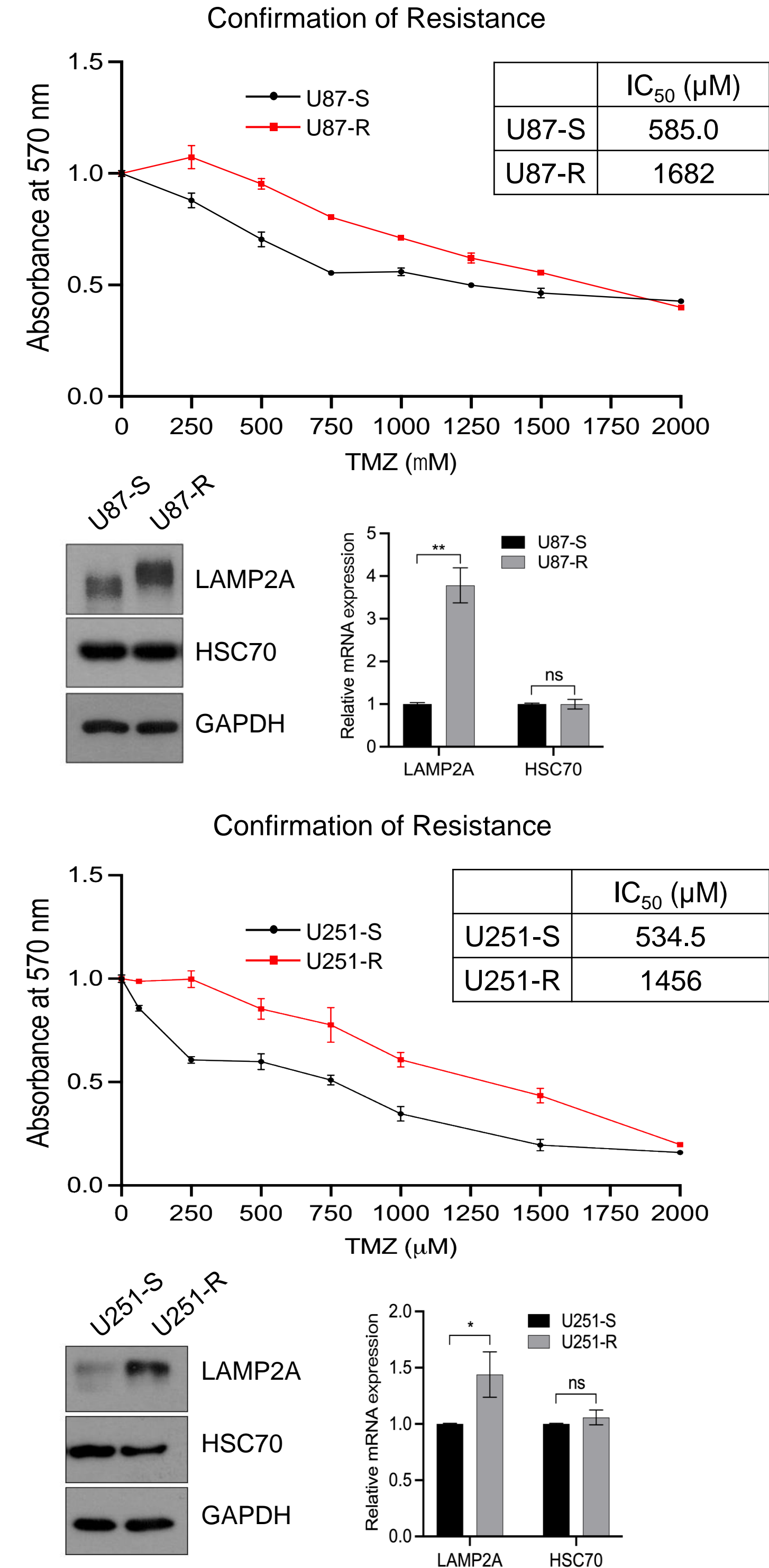
- Response of GBM cells to TMZ was detected by MTT assay. The mRNA and protein expression levels of LAMP2A (indicating factor of CMA) were measured using RT-qPCR, western blotting or IHC, respectively.
- C57BL/6 mice were injected subcutaneously with GL261 cells. Two weeks later, tumor-bearing mice received TMZ (15mg/kg) treatment for 2 weeks (3 days/week).

## Results

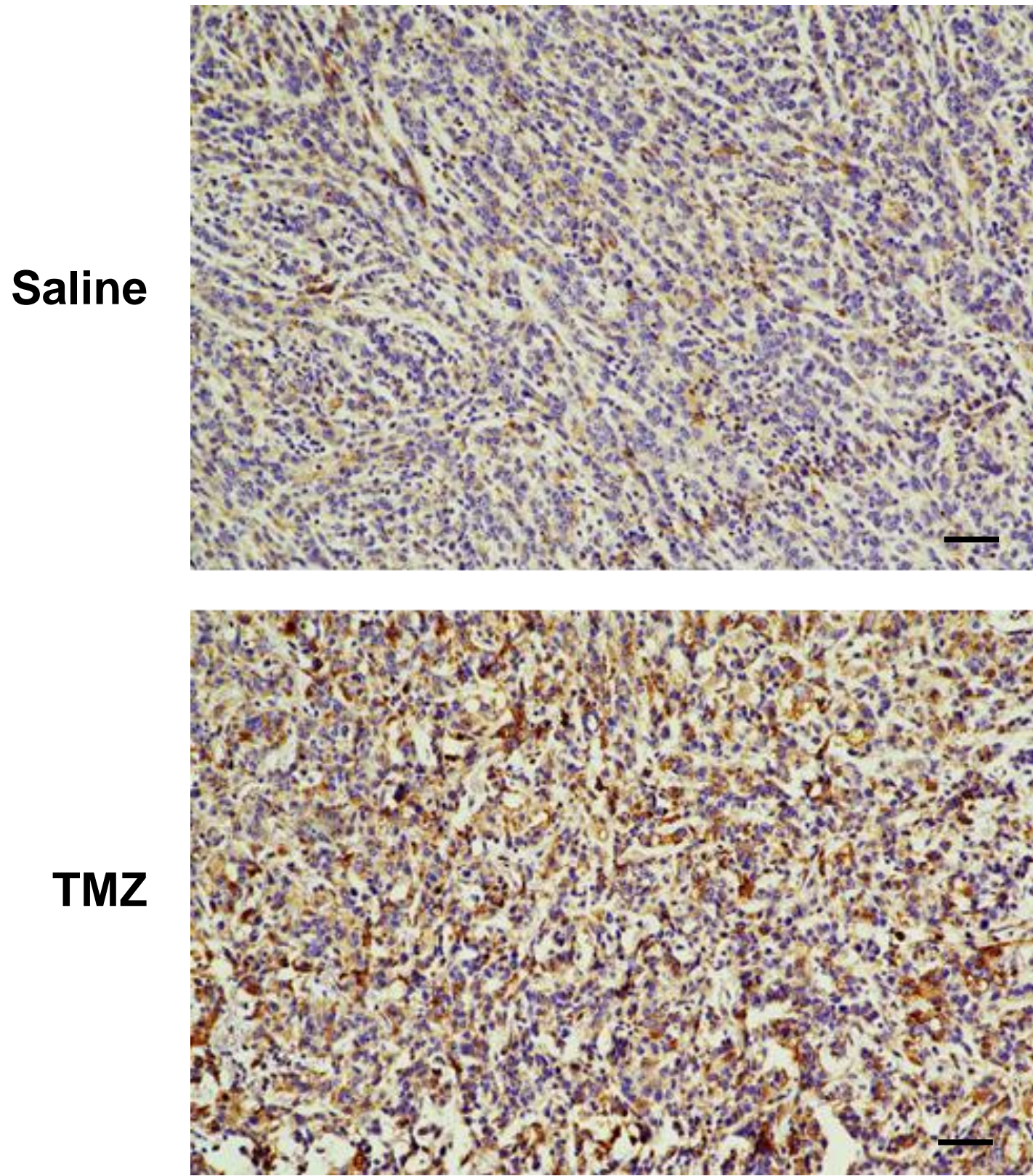
### 1. Higher LAMP2 gene expression in high grade recurrent glioma



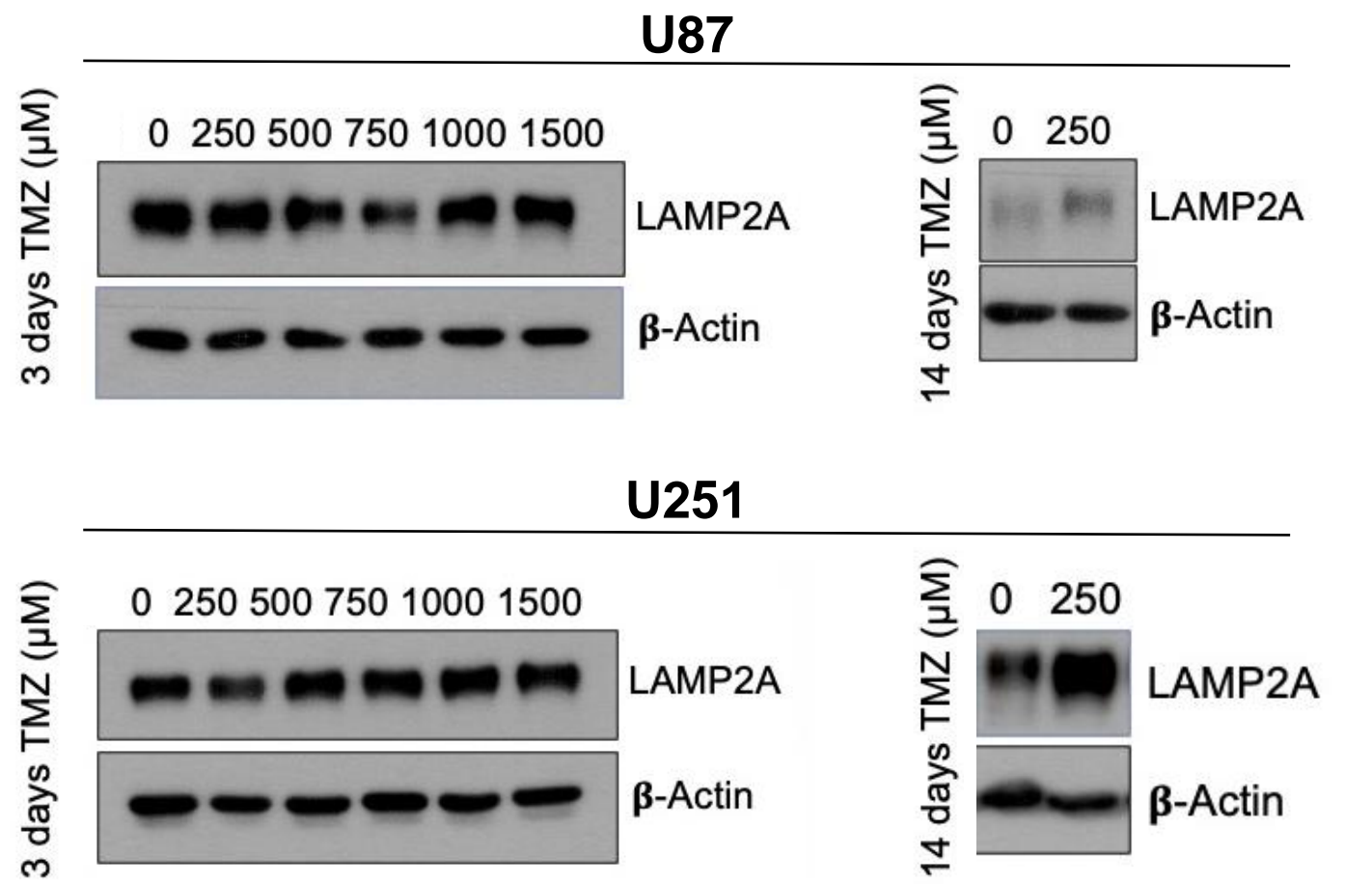
### 2. Higher LAMP2A (indicator of CMA) expression in TMZ-resistant GBM cells



### 3. Two-week TMZ treatment induced CMA *in vivo*



### 4. Upregulated LAMP2A might be a result of long-term TMZ treatment



## Conclusions

- LAMP2 gene was upregulated in recurrent GBM samples in the CGGA database.
- Both the mRNA and protein expressions of LAMP2A were elevated in TMZ resistant U87 and U251 GBM cell lines.
- Two weeks TMZ treatment could upregulate CMA both *in vivo* and *in vitro*, while 3 days TMZ treatment was not able to change the expression level of LAMP2A, even with higher TMZ concentration.

## Discussion

Upregulated LAMP2A might be a result of long term TMZ treatment, which was not dose dependent. Characterizing its consequence may help to enhance the efficacy of TMZ treatment.

## References

[1] Koukourakis, Michael I et al. "Therapeutic interactions of autophagy with radiation and temozolomide in glioblastoma: evidence and issues to resolve." *British journal of cancer* vol. 114,5 (2016): 485-96. doi:10.1038/bjc.2016.19

[2] Andrade-Tomaz, Marina et al. "The Role of Chaperone-Mediated Autophagy in Cell Cycle Control and Its Implications in Cancer." *Cells* vol. 9,9 2140. 22 Sep. 2020, doi:10.3390/cells9092140